Basic Summary of Recent Significant Cerebrovascular Studies

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Most studies have found a rupture rate for intracranial aneurysms of about 1% annually. The ISUIA (International Study of Unruptured Intracranial Aneurysms) was initially published in NEJM in 1998. This study (retrospective data on 1500 patients over 21 years) found an extremely low rate of rupture for aneurysms < 10mm in size (0.05% annual risk for rupture). In patients who had previously suffered a SAH from another aneurysm (Group II), the study found the risk for a remaining aneurysm rupturing was 0.5%.

There have been significant issues raised with the validity of ISUIA. Given the rupture rate indicated in the first ISUIA study, there would need to be an incidence of aneurysms of 20% in the general population to match the incidence of SAH. Aneurysms less than 10mm in size in Group I (no prior SAH) were not stratified with regard to risk for rupture. Only 18% of patients in Group I had aneurysms between 6-9mm in size and intracavernous aneurysms were included. In the Cooperative Study of Intracranial Aneurysms and SAH involving over 6,000 patients, the critical size for rupture was found to be 7-10mm.

Also, in the ISUIA study, the morbidity of surgical treatment was higher than anticipated and was directly related to age (prospective data on 1,100 patients over 4 years). This mainly involved cognitive alteration. Surgical M&M for incidental aneurysms was found to be 6.5% in patients < 45 years old, 14.4% in patients 45-65 years old, and 32% in patients >65 years old. Therefore, in the ISUIA, the risk for rupture appeared much lower than previously reported and the risks for treatment much higher. However, in the surgical group, there were a higher proportion of aneurysms in the posterior circulation compared to the natural history group and nearly 50% were larger than 1 centimeter.

The ISUIA was updated in Lancet 2003. This provided prospective data on natural history information on approximately 1,600 patients followed for 4 years. They are hoping to extend the study further with additional funding. In this study, 7mm appeared to be a critical size for rupture in group I patients. In aneurysms < 7mm, the risk for rupture remained low (0.1% annually). Aneurysms at the basilar apex and PCoA appeared to have a significantly higher rate for rupture than aneurysms in other locations. The rupture rate remained higher for aneurysms of all sizes in Group II patients. In those who did suffer a hemorrhage, the mortality rate was exceptionally high at 65%.

The ISAT (International Subarachnoid Aneurysm Trial) randomized approximately 20% of over 9,000 patients with a ruptured aneurysm to either endovascular or surgical treatment. Thus, in nearly 80% of patients, there was a clear recommendation that the aneurysm be treated by one or the other method. In the 20% of patients in whom either

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treatment method was felt to be acceptable, there was an absolute risk reduction of 6.9% for patients in the endovascular group at one year follow-up. However, the rebleed rate was nearly three times greater in the endovascular group and they also required re-treatment four times as commonly as the surgical group during the relatively short follow-up period. Long term analysis of the angiographic results is anticipated. Obviously, these results are not applicable to any ruptured intracranial aneurysm, but only to those in which either method of obliteration is felt to be equivalent. This study addresses safety but does not address the question of equivalence with regard to durability and completeness of obliteration.

At present, there is a general consensus that endovascular treatment is safer than surgical intervention in most situations where either approach could be utilized. However, the major issues regarding endovascular therapy involve efficacy and durability. In general, the complete occlusion rate with endovascular treatment is only 50-55%. The recurrence rate is 20-40%. The longer the follow-up period, the more likely that recurrences will be detected. Endovascularly treated aneurysms should be monitored for at least 3 years. Filling within the body of the aneurysm, coil compaction, and aneurysm growth/recurrence should be retreated. The natural history of incomplete endovascular treatment (neck remnant or incomplete coiling at the base) is not well understood at the present time (Murayama et al, J Neurosurg 2003; Raymond et al, Stroke 2003).

Recently, Lanzino et al. (J Neurosurg 104, 2006) reviewed their experience with an approach where clipping and coiling were felt to be complementary treatment techniques. Currently, they feel that the majority of ruptured MCA, small PCoA, and small ACoA aneurysms should be considered for primary surgical treatment, unless the patient is elderly

In my opinion, the following issues need to be considered when counseling a patient with an incidental aneurysm:

1. Most aneurysms less than 7mm in size have a very low risk for rupture. The presence of irregularities or blebs and/or location at the basilar apex or PCoA may be more dangerous.
2. Younger age and psychological issues (the patient's psychological tolerance to harbor an intracranial aneurysm) may influence one toward more aggressive strategies (van der Schaaf et al, Stroke 2002).
3. Older patients have an increased morbidity with treatment, especially surgical.
4. Endovascular treatment is generally a safer procedure. However, the issues of incomplete treatment and durability are still major concerns which need to be settled. Most facilities or institutions will have a preferential strength for either an endovascular or surgical approach. This will influence the treatment paradigm at any given facility and should rightly be part of the decision making process.

ISUIA I (NEJM 1998)

Prospective data collected on 1100 patients over 4 years analyzed to determine treatment M&M.
Retrospective data on 1500 patients over 21 years to assess natural history.
Neither arm was prospective, randomized, or controlled.

Conclusions from ISUIA I:

Group I (no prior SAH)

<10mm	0.05% risk annually
10-24mm	0.5% risk annually
>25mm	6% risk in first year

Group II (prior SAH)

<10mm	0.5% risk annually
>10mm	1% risk annually

Increased morbidity and mortality from treatment than previously recognized.*
(*increased morbidity secondary to mental status changes)

30 day M&M	13.6-17.5%
1 year M&M	13.1-15.7%
<45 years old	6.5%
45-65 years old	14.4%
>65 years old	32%

ISUIA II (Lancet 2003)

Prospective data on natural history of UIA and results of endovascular and surgical treatment.

- December 1991- 1998
- 4060 patients enrolled
    - 50% (2035) before 1996
    - 43% (1775) 1997-1998

1692 patients (1077patients in group I, 615 in group II) managed conservatively for a mean of 4.1 years (SD=2.0) for 6544 patient years. 727 patients removed from follow-up (534 who were treated and 193 who died).

Rupture in previously UIA during *mean* 4.1 year follow-up*.

Group 1 (no prior SAH)	41 patients	
<7mm	2	(0.1% annually)
7-9mm	5	
Group 2 (prior SAH)		
<7mm	7	
7-9mm	1	

****number at risk for rupture by 6 years was very small (1072 to 61 in group 1 and 608 to 41 in group 2). Mortality in 51 with subsequent hemorrhage was 65%.***

Predictors of aneurysmal hemorrhage

Size

7-12 mm maximum diameter

Location

Posterior Communicating Artery
Basilar Apex

Factors affecting surgical outcome

Age (increased for patients about 50 years and older, substantially increased after age 60-70 years)

Aneurysm diameter > 12mm
Posterior circulation aneurysm
Previous ischemic cerebrovascular disease
Aneurysmal symptoms other than rupture

Surgical morbidity in ISUIA II:

Intra-operative rupture	6%
Intracranial hemorrhage	4%
Cerebral infarction	11%
Morbidity and mortality	***12.6% group 1***
	10.1% group 2

Endovascular morbidity in ISUIA II:

Periprocedural hemorrhage	2%
Cerebral infarction	5%
Morbidity and mortality	***9.1% group 1***
	9.5% group 2

Endovascular result with GDC coiling:

Complete obliteration	*55%*
Partial obliteration	24%
No obliteration	18%
Unknown	3%

ISAT

9,278 patients with ruptured aneurysms

2,143 randomized (nearly 80% not randomized)

30.6% poor outcome at 1 year following surgery
23.7% poor outcome at 1 year following coiling
6.9% absolute risk reduction (22.6% relative risk reduction)

Rebleed during short term follow-up: 2.6% (GDC) vs. 0.9% (surgery)
Four times more GDC patients required additional treatment (121/1005 v. 33/968)

Murayama, Nien, Duckwiler,et al. **J Neurosurg 98:** 959-966, 2003

Complete occlusion	55%	Group A: first 5 yr (251)
Neck remnant	35.4%	
Incomplete embolization	3.5%	Group B: last 6 yr (665)
Unsuccessful attempt	5%	

Group B results:

Small aneurysm/small neck	***72.9% complete***	***23.4% neck remnant***
Small aneurysm/wide neck	40.8% complete	46.1% neck remnant
Large aneurysm	41.4% complete	42.2% neck remnant
Giant aneurysm	37.5% complete	57.5% neck remnant

Recanalization ***20.9% (group B)***

Small aneurysm/small neck	5.8%	(1.1% complete, 20.7% remnant)
Small aneurysm/wide neck	18.2%	(7.5%, 29.4%)
Large aneurysm	37.7%	(30%, 44.4%)
Giant aneurysm	52.9%	(42.9%, 60%)

Delayed rupture 4.1% group A 0.5% group B

Complications: 8.4% (2.4% embolization, 2.3% perforation, 2% parent artery occlusion)

Raymond et al ***Stroke 2003*** Recurrence rate with GDC coils

Approximately 33.6% recurrence rate at 12 months.
Major recurrence = 20.7% at 16 months.
49% of major recurrences were retreated.
48% developed a second recurrence.

In patients with long term follow-up,

40%	*recurrence rate*
24%	*major recurrence*

Factors associated with recurrence after GDC
Treatment during the acute phase following SAH
Wider neck of aneurysm

Suboptimal initial angiographic result

Length of follow-up

50% of all recurrences detected at 6 months

96% of all recurrences detected at 3 years.